L2: Entry 3 of 11 File: PGPB Nov 28, 2002

DOCUMENT-IDENTIFIER: US 20020177770 A1
TITLE: Assessing the condition of a joint and assessing cartilage loss

Summary of Invention Paragraph (9):
[0010] Magnetic resonance imaging (MRI) is an accurate non-invasive imaging technique for visualization of articular cartilage in osteoarthritis, particularly in knees. However, current MRI techniques cannot provide information on the relationship between the location of the cartilage loss and variations in the load bearing areas during the walking cycle. This information is important since it has been shown that dynamic loads during walking are related to the progression of knee OA. Thus, the ability to locate cartilage defects or areas of cartilage thinning relative to the load bearing areas of the knee could be valuable in evaluating factors influencing the progression of osteoarthritis.

Summary of Invention Paragraph (26):
[0027] 16. Beaulieu C F, Hodge D K, Thabit G, Lang P K, Bergman A G: Dynamic imaging of glenohumeral instability with open MRI. Int. Society for Magnetic Resonance in Medicine, Sydney, Australia, 1998.

Summary of Invention Paragraph (35):
[0036] 25. Broderick L S, Turner D A, Renfrew D L, Schnitzer T J, Huff J P, Harris C: Severity of articular cartilage abnormality in patients with osteoarthritis: evaluation with fast spin-echo MR vs arthroscopy. AJR 1994; 162: 99-103.

Summary of Invention Paragraph (46):
[0047] 36. Dumoulin C L, Souza S P, Darrow R D: Real-time position monitoring of invasive devices using magnetic resonance. Magn Reson Med 1993; 29: 411-5.

Summary of Invention Paragraph (53):
[0054] 43. Ghosh S, Newitt D C, Majumdar S: Watershed segmentation of high resolution articular cartilage image. International Society for Magnetic Resonance in Medicine, Philadelphia, 1999.

Summary of Invention Paragraph (56):
[0057] 46. Hargreaves B A, Gold G E, Conolly S M, Nishimura D G: Technical considerations for DEFT imaging. International Society for Magnetic Resonance in Medicine, Sydney, Australia, Apr. 17-24, 1998.

Summary of Invention Paragraph (57):
[0058] 47. Hargreaves B A, Gold G E, Lang P K, Bergman G, Conolly S M, Nishimura D G: Imaging of articular cartilage using driven equilibrium. International Society for Magnetic Resonane in Medicine, Sydney, Australia, Apr. 17-24, 1998.

Summary of Invention Paragraph (62):
[0063] 52. Irarrazabal P, Nishimura D G: Fast three-dimensional magnetic resonance imaging. Mag Res Med 1995; 33: 656-662.

Summary of Invention Paragraph (67):
[0068] 57. Lang P, Alexander E, Andriacchi T: Funcional joint imaging: a new technique integrating MRI and biomotion studies. International Society for Magnetic Resonance in Medicine, Denver, Apr. 18-24, 2000.

Summary of Invention Paragraph (69):
[0070] 59. Lang P, Hargreaves B A, Gold G, et al.: Cartilage imaging: comparison of driven equilibrium with gradient-echo, SPGR, and fast spin-echo sequences.

International Society for Magnetic Resonance in Medicine, Sydney, Australia, Apr. 17-24, 1998.

Summary of Invention Paragraph (80):
[0081] 70. Noll D C, Nishimura D, Macovski A: Homodyne detection in magnetic resonance imaging. IEEE Trans Med Imag10 1991; 10 (2): 154-163.

Summary of Invention Paragraph (88):
[0089] 78. Potter H G, Linklater J M, Allen A A, Hannafin J A, Haas S B: Magnetic resonance imaging of articular cartilage in the knee: an evaluation with use of fast-spin-echo imaging. J Bone Joint Surg 1998; 80-A(9): 1276-1284.

Summary of Invention Paragraph (100):
[0101] 90. Shoup R R, Becker E D: The driven equilibrium Fourier transform NMR technique: an experimental study. J Mag Res 1972; 8.

Summary of Invention Paragraph (111):
[0112] 101. Tieschky M, Faber S, Haubner M, et al.: Repeatability of patellar cartilage thickness patterns in the living, using a fat-suppressed magnetic resonance imaging sequence with short acquisition time and three-dimensional data processing. J Orthop Res 1997; 15(6): 808-813.

Summary of Invention Paragraph (113):
[0114] 103. Tsai J, Ashjaee S, Adalsteinsson E, et al.: Application of a flexible loop-gap resonator for MR imaging of articular cartilage at 3.0T. International Society for Magnetic Resonance in Medicine, Denver, Apr. 18-24, 2000.

Summary of Invention Paragraph (119):
[0120] 109. Yao L, Gentili A, Thomas A: Incidental magnetization transfer contrast in fast spin-echo imaging of cartilage. J Magn Reson Imaging 1996; 6 (1): 180-184.

Summary of Invention Paragraph (127):
[0127] One aspect of this invention is a method for assessing the condition of a cartilage. The method comprises obtaining an image of a cartilage, (preferably a magnetic resonance image), converting the image to a three-dimensional degeneration pattern, and evaluating the degree of degeneration in a volume of interest of the cartilage. By performing this method at an initial time T, and a later time T.sub.2, one can determine the change in the volume of interest and evaluate what steps to take for treatment.

Summary of Invention Paragraph (144):
[0144] A method for assessing the condition of the knee joint of a human patient, wherein the knee joint comprises cartilage and associated bones on either side of the joint, which method comprises (a) obtaining the patient's magnetic resonance imaging (MRI) data of the knee showing at least the bones on either side of the joint, (b) segmenting the MRI data from step (a), (c) generating a geometrical representation of the bone of the joint from the segmented MRI data, (d) assessing the patient's gait to determine the load pattern or the cartilage contact pattern of the articular cartilage in the joint during the gait assessment, and (e) correlating the load pattern or cartilage contact pattern obtained in step (d) with the geometrical representation obtained in step (c).

Brief Description of Drawings Paragraph (14):
[0161] FIG. 11A shows a 2D cartilage thickness map where a proton density fast spin-echo MR image demonstrates a focal cartilage defect in the posterior lateral fermoral condyle (black arrows). White arrows indicate endpoints of the thickness map.

Detail Description Paragraph (19):
[0195] In obtaining an image of the cartilage of a joint in a mammal, a number of internal imaging techniques known in the art are useful for electronically generating a cartilage image. These include magnetic resonance imaging (MRI), computed tomography scanning (CT, also known as computerized axial tomography or CAT), and ultrasound imaging techniques. Others may be apparent to one of skill in the art. MRI techniques are preferred.

Detail Description Paragraph (25):
[0201] Routine MRI pulse sequences available for imaging tissue, such as cartilage, include conventional T1 and T2-weighted spin-echo imaging, gradient recalled echo (GRE) imaging, magnetization transfer contrast (MTC) imaging, fast spin-echo (FSE) imaging,

contrast enhanced imaging, rapid acquisition relaxation enhancement, (RARE) imaging, gradient echo acquisition in the steady state, (GRASS), and driven equilibrium Fourier transform (DEFT) imaging. As these imaging techniques are well known to one of skill in the art, e.g. someone having an advanced degree in imaging technology, each is discussed only generally hereinafter. While each technique is useful for obtaining a cartilage degeneration pattern, some are better than others.

Detail Description Paragraph (32):
[0208] Fast Spin-Echo Imaging

Detail Description Paragraph (33):
[0209] Fast spin-echo imaging is another useful pulse sequence to evaluate articular cartilage. Incidental magnetization transfer contrast contributes to the signal characteristics of articular cartilage on fast spin-echo images and can enhance the contrast between cartilage and joint fluid. Sensitivity and specificity of fast spin-echo imaging have been reported to be 87% and 94% in a study with arthroscopic correlation.

Detail Description Paragraph (35):
[0211] The use of gadolinium for imaging of articular cartilage has been applied in several different forms. Direct magnetic resonance (MR) arthrography, wherein a dilute solution containing gadolinium is injected directly into the joint, improves contrast between cartilage and the arthrographic fluid. Indirect MR arthrography, with a less invasive intravenous injection, can also been applied. Gadolinium enhanced imaging has the potential to monitor glycosaminoglycan content within the cartilage, which may have implications for longitudinal evaluations of injured cartilage.

Detail Description Paragraph (36):
[0212] Driven Equilibrium Fourier Transform

Detail Description Paragraph (37):
[0213] Another 3D imaging method that has been developed is based on the driven equilibrium fourier transform (DEFT) pulse sequence (U.S. Pat. No. 5,671,741), and is specifically designed for cartilage imaging. DEFT provides an effective tradeoff between T2/T1 weighting and spin density contrast that delineates the structures of interest in the knee. Contrast-to-noise ratio between cartilage and joint fluid is greater with DEFT than with spoiled gradient echo (SPGR). DEFT is an alternative approach to SPGR. DEFT contrast is very well suited to imaging articular cartilage. Synovial fluid is high in signal intensity, and articular cartilage intermediate in signal intensity. Bone is dark, and lipids are suppressed using a fat saturation pulse. Hence, cartilage is easily distinguished from all of the adjacent tissues based on signal intensity alone, which will greatly aid segmentation and subsequent volume calculations.

Detail Description Paragraph (39):
[0215] DEFT was compared with a fast spin-echo (FSE), a gradient-echo (GRE), and a spoiled gradient-echo (SPGR) sequence with parameters similar to the ones published by Disler et al. The patella was scanned in 10 normal volunteer knees using a 1.5T whole-body system (GE Signa) with a 3 inch surface coil. All images were acquired with field of view (FOV) 10.times.10 cm, matrix 256.times.256 elements, slice thickness 4 mm using fat-saturation. DEFT (400/15 [TRITE in msec], 2 NEX (number of excitations), FSE (3500/15, echo train length [ETL] 8, 2 NEX (number of excitations), FSE (3500/15, ETL 4, 2 NEX), GRE (400/20, 30.degree., 2 NEX), and SPGR (50/15, 30.degree. [flip angle], 2 NEX) images were obtained. Contrast-to-noise ratios (CNR) between cartilage and joint fluid were calculated as:

Detail Description Paragraph (48):
[0222] In summary, Driven Equilibrium Fourier Transform is a pulse sequence preferred for cartilage imaging that provides higher contrast-to-noise ratios and contrast between cartilage and joint fluid than SPGR, GRE, and FSE sequences. Cartilage morphology is better delineated with DEFT sequences than with SPGR, GRE, and FSE images. The combination of high anatomic detail and high cartilagejoint fluid CNR and contrast may render this sequence particularly useful for longitudinal studies of cartilage in patients with osteoarthritis.

Detail Description Paragraph (58):
[0232] Thus, one embodiment of the invention is a skin reference marker that can be used in the assessment of the condition of a joint of a human. Multiple skin reference markers can be placed upon one or more limbs of a patient prior to internal imaging and

external imaging. Each skin reference marker comprises a material detectable by an imaging technique, a container for the material in which the container preferably has multiple surfaces, a means for affixing the container to the skin (e.g. an adhesive placed on at least one surface of the container in an amount sufficient to adhere the container to the skin of a human), and a reflective material (preferably retro-reflective) placed on another surface of the container located away from the adhesive. Several imaging techniques can be used that are able to detect the marker. For example, magnetic resonance imaging is preferred, but, ultrasound, or X-ray are also useful. In the case of X-ray, further manipulations must be performed in which multiple X-ray images are assimilated by a computer into a 2 dimensional cross-sectional image called a Computed Tomography (CT) Scan. The material detectable by an imaging can be either in a liquid form or a solid form. The material can be any imaging contrast agent or solution, e.g. a paramagnetic material. The material can be a lanthanide, such as one belonging to the yttrium group of rare earth metals. More specifically, the material can be gadolinium. The shape of the container can be any shape allowing it to be placed on the skin of a human. For example, it can be cubical, spherical, elliptical, discoid or cylindrical. The size of the container can be any size, but optimally a size allowing it to be recorded by an imaging machine. The longest dimension of the container can be up to 5.0 cm, but preferably is about 0.25 to 2.0 cm. The reflective or retro-reflective material can be any material that is able to reflect light directly back to the source of the light so that the position of the reference marker is captured by the opto-electrical recording means, e.g. a video camera. 3M Corporation makes several retro-reflective materials.

Detail Description Paragraph (60):
[0234] Once a magnetic resonance image is obtained, it can be manipulated to improve the image by reducing unwanted, non-cartilage images.

Detail Description Paragraph (113):
[0285] A biochemical component includes, but is not limited to, glycosaminoglycan, water, sodium, or hyaluronic acid. Biochemical data can be generated with other magnetic resonance based techniques including the use of paramagnetic and other contrast media and sodium rather than proton MR imaging. Other imaging tests such as positron emission tomography scanning can also be used for this purpose. Thus, one aspect of this invention is a method for providing a biochemically-based map of joint cartilage. The method comprises

Detail Description Paragraph (156):
[0328] Since the algorithm for 3D surface registration of the femoral condyles also computes the surface normals for the medial and lateral femoral condyles on a pixel-by-pixel basis, it can form the basis for developing maps of cartilage thickness. FIG. 11 shows an example of a 2D map of cartilage thickness derived from the surface normals of the lateral femoral condyle. FIG. 11A shows a proton density fast spin-echo MR image that demonstrates a focal cartilage defect in the posterior lateral femoral condyle (black arrows). White arrows indicate endpoints of thickness map. FIG. 11B is a 2D cartilage thickness map that demonstrates abrupt decrease in cartilage thickness in the area of the defect (arrows). The A thickness between neighboring pixels can be used to define the borders of the cartilage defect. Note diffuse cartilage thinning in area enclosed by the astericks (*).

Detail Description Paragraph (281):
[0436] As pointed out at numerous places in the specification, the use of external reference markers that are detectable by both MRI and optical techniques can be an important and useful tool in the method of this invention. The use of the reference markers can form the basis for an aspect of this invention that is a method for correlating cartilage image data, bone image data, and/or opto-electrical image data for the assessment of the condition of a joint of a human. This method comprises, obtaining the cartilage image data of the joint with a set of skin reference markers placed externally near the joint, obtaining the bone image data of the joint with a set of skin reference markers placed externally near the joint, obtaining the external bone image data opto-electrical image data of the joint with a set of skin reference markers placed externally near the joint. Using the skin reference markers, one can then correlate the cartilage image, bone image and opto-electrical image with each other, due to the fact that each skin reference marker is detectable in the cartilage, bone and opto-electrical data. The cartilage image data and the bone image data can be obtained by magnetic resonance imaging, positron emission tomography, single photon emission computed tomography, ultrasound, computed tomography or X-ray. Typically, MRI will be preferred. In the case of X-ray, further manipulations must be performed in which multiple X-ray images are assimilated by a computer into a 2 dimensional

cross-sectional image called a Computed Tomography (CT) Scan. The opto-electrical image data can be obtained by any means, for example, a video camera or a movie camera. Multiple skin reference markers can be placed on one or more limbs of the patient prior to imaging. The skin reference markers are described hereinbefore.

Detail Description Paragraph (302):
[0457] Cartilage loss can be assessed by subtracting two images of the same individual that were acquired at different times to and t.sub.2. The same technique can be used to measure cartilage gain for example when a patient is undergoing chondro-regenerative treatment. Typically, the images are three-dimensional data sets (e.g. magnetic resonance images) and will have similar contrast (e.g. cartilage is shown in bright, bone is shown in dark). For each voxel, the difference of the intensities (gray values) at times t.sub.1 and t.sub.2 is computed. The difference image is then composed of the absolute values of the differences for each voxel.

Detail Description Paragraph (311):
[0466] The invention provides for techniques to assess biomechanical loading conditions of articular cartilage in vivo using magnetic resonance imaging and to use the assessment as an aid in providing therapy to a patient. In one embodiment, biomechanical loading conditions can be assessed in normal articular cartilage in various anatomic regions. In the knee joint, these anatomic regions include the posterior, central, and anterior medial femoral condyle, the posterior, central, and anterior medial tibial plateau, the posterior, central, and anterior lateral femoral condyle, the posterior, central, and anterior lateral tibial plateau, the medial and lateral aspect of the trochlea, and the medial and lateral facet and the median ridge of the patella. Since biomechanical loading conditions are assessed in vivo based on the anatomic features of each individual patient, a risk profile can be established for each individual based on the biomechanical stresses applied to cartilage. In this fashion, patients who are at risk for developing early cartilage loss and osteoarthritis can be identified. For example, patients with a valgus or varus deformity of the knee joint will demonstrate higher biomechanical stresses applied to the articular cartilage in the medial femorotibial or lateral femorotibial or patellofemoral compartments than patients with normal joint anatomy. Similarly, patients with disturbances of joint congruity will demonstrate higher biomechanical stress applied to certain regions of the articular cartilage. Such disturbances of joint congruity are often difficult to detect using standard clinical and imaging assessment. The amount of stress applied to the articular cartilage can be used to determine the patient's individual prognosis for developing cartilage loss and osteoarthritis. In another embodiment, biomechanical loading conditions can be assessed in normal and diseased articular cartilage. An intervention that can alter load bearing can then be simulated. Such interventions include but are not limited to braces, orthotic devices, methods and devices to alter neuromuscular function or activation, arthroscopic and surgical procedures. The change in load bearing induced by the intervention can be assessed prior to actually performing the intervention in a patient. In this fashion, the most efficacious treatment modality can be determined. For example, a tibial osteotomy can be simulated in the manner and the optimal degree of angular correction with regard to biomechanical loading conditions of normal and diseased cartilage can be determined before the patient will actually undergo surgery.

Detail Description Paragraph (328):
[0483] (a) obtaining the patient's magnetic resonance imaging (MRI) data of the knee showing at least the cartilage on at least one side of the joint,

Detail Description Paragraph (334):
[0489] (a) obtaining the patient's magnetic resonance imaging (MRI) data of the knee showing at least the bones on either side of the joint,

CLAIMS:

7. The method claim 1, wherein the three-dimensional map of cartilage is obtained by a magnetic resonance imaging (MRI) technique.

9. The method of claim 7, wherein the MRI technique employs a gradient echo, spin echo, fast-spin echo, driven equilibrium founier transform, or spoiled gradient echo technique.